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Brief Clinical Report

Follow-Up of a Familial Translocation t(10;16) With an Unusual Segregation Pattern

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Bofinger et al. [Am J Med Genet 38:1–8, 1991] reported on a four-generation family with an unusual segregation pattern involving a translocation t(10;16)(q26.3;p13.1). All relatives either had a balanced or unbalanced translocation. We report on five additional relatives, none of whom have a normal karyotype. This unusual segregation pattern may be due to chance or be the result of meiotic drive. © 1996 Wiley-Liss, Inc.

KEY WORDS: translocation, segregation distortion, meiotic drive

INTRODUCTION

Bofinger et al. [1991] reported on a familial translocation t(10;16)(q26;p13.1) where all relatives either had a balanced or unbalanced translocation; no normal karyotypes were observed. Six children who inherited the unbalanced translocation had multiple congenital anomalies and mental retardation. We present additional information on this family to report that the unusual segregation pattern has continued.

At her initial clinic visit, the consultand (III-12) (Fig. 1) was a 30-year-old G2SAb1 woman. Amniocentesis in her first pregnancy (IV-7) demonstrated a balanced translocation 46,XX,t(10;16)(q26.3;p13.1)mat. A second pregnancy (IV-8) resulted in an unkaryotyped first trimester miscarriage.

The patient declined CVS and amniocentesis in her third pregnancy (IV-9). Maternal serum AFP/hCG/estriol levels were normal at 16.5 weeks. Ultrasound examination at 20 weeks demonstrated a single fetus with left multicystic renal dysplasia, bilateral club foot, and a two-vessel umbilical cord. Amniotic fluid volume was normal. At approximately 32 weeks, bilateral pleural effusions developed, which were drained via thoracocentesis. The fetus was not hydropic. Chromosome studies from pleural fluid cells demonstrated an unbalanced karyotype, 46,XX,+der(10)t(10;16) (q26.3;p13.1)mat. The fetus died at 34 weeks.

Autopsy showed anomalies consistent with the unbalanced karyotype, including microcephaly, posterior midline cleft palate, dislocated left hip, bilateral talipes equinovarus, bilateral tapering digits, "digitalized" thumbs, bilobed right lung, persistent left superior vena cava which drained to a dominant hemizygous vein, bilateral hydronephrosis with left microcystic renal dysplasia, normal urinary bladder, and left single umbilical artery (Table I). Single umbilical artery was the only anomaly found in this baby which was not reported in other relatives with unbalanced karyotypes.

In her fourth pregnancy (IV-10), the patient underwent amniocentesis at 15.4 weeks. Chromosome studies indicated a balanced translocation, 46,XY,t(10;16)(q26.3;p13.1)mat. The child was phenotypically normal at birth.

Two other relatives (III-5, III-7) each have had one child (IV-5, IV-6) since the original pedigree was published. Both children are phenotypically normal balanced translocation carriers.

DISCUSSION

For this family, the risk of having unbalanced offspring is close to 50%. The anomalies described in the fetus with the unbalanced karyotype are consistent with the phenotype of other relatives with the unbalanced karyotype. The defects are similar to previously reported cases of trisomy 16p, including microcephaly, cleft palate, tapering fingers, club foot, single umbilical artery, and cardiac defects [Léonard et al., 1992; O'Connor and Higgins, 1992]. There is some overlap of features with del(10q), including microcephaly, heart defects, and urinary tract anomalies [Gorinati et al., 1989; Wulfsberg et al., 1989].

Estimating the reproductive risks for balanced translocation carriers is difficult. Most studies have focused on the risk either for producing a liveborn child with an unbalanced karyotype or miscarriage [Neri et al., 1983; Boué and Gallano, 1984; Daniel et al., 1989; Midro et al., 1992; Cans et al., 1993]. Cytogenetic studies of sperm from carriers of other translocations have usually found a 1:1 ratio of balanced to normal

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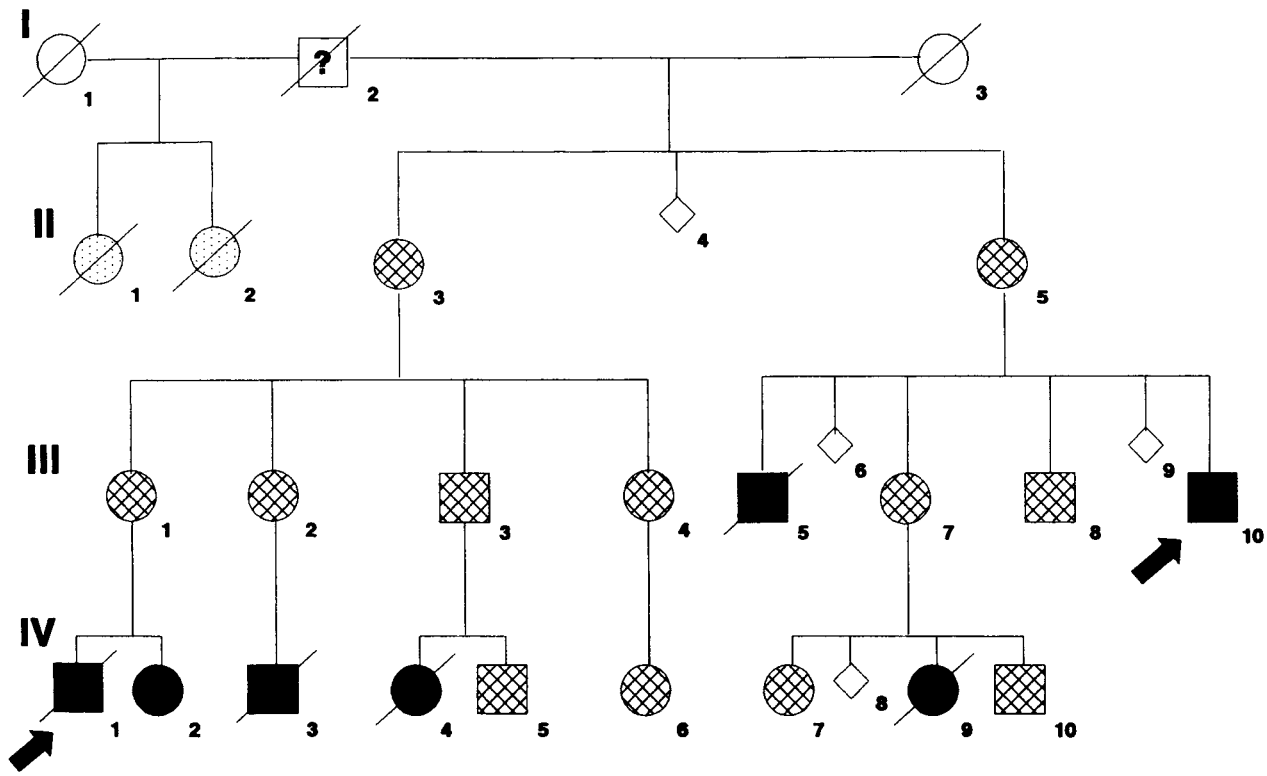

Fig. 1. Pedigree illustrating inheritance translocation t(10;16)(q26.3;p13.1) in this family, updated and adapted from Bofinger et al. [1991], Figure 1. ■, dup(16)(p13.1-pter),del(10)(q26.3-qter); ⊗, t(10;16)(q26.3;p13.1); ⊗, presumed dup(16)(p13.1-pter),del(10)(q26.3-qter); ○, Presumed normal partner; ?, presumed t(10;16)(q26.3;p13.1); ◇, unkaryotyped spontaneous miscarriage.

TABLE I. Clinical in Relatives With dup(16p) and del(10q)*

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Present case
Surviving age	2 days[a]	17 years	5 months[a]	16 months[a]	2 years	4 months[a]	SB[b]
Sex	M	M	M	M	F	F	F
Gestation	39	40	38	32	38	41	30
Birthweight	2183	2605	2720	2330	4000	4080	2230
Birth OFC (cm)		32.5	31.5	31	32	35.5	29
Fetal hydrops				+	+	+	−
Respiratory distress	+	+	+	+	+	+	n/a
Failure to thrive		+	+	+	+	+	n/a
DD/MR		+	+	+	+	+	n/a
Microcephaly		+	+	+	+	−	+
Hypotonia	+	+	+	+	+	+	n/a
Narrow palpebral fissures		+	+	+	+	+	−
Upward slanted fissures			+	+	+	+	+
Epicanthal folds	+	−	−	+	+	+	+
Abnormal pinnae	+	+	+	+	+	+	−
Apparently low-set ears	+	+	+	+	+	+	−
Cleft palate	+	+	−	−	−	+	+
Redundant neck folds		+	+	+	+	+	−
Congenital heart defect	−	+	+	+	+	+	+[c]
Ventilator dependent		−	+	+	−	+	n/a
Thumbs/radial ray defect	+	+	+	+	+	−	+
Clinodactyly V				+	+	+	−
Club feet	+	+	−	+	−	−	+
Hypospadias	+	+	−	−			−
Cryptorchidism		+	−	+			n/a
Kidneys dysplastic	+	−	−	−	−	−	+
Inguinal herniae	−	+	+	+	+	−	n/a
Sparse white hair				+	+	−	n/a
Single umbilical artery							+

*Adapted from Bofinger et al. [1991], Table I.
[a] Age at death.
[b] Stillborn.
[c] Persistent left superior vena cava.

karyotypes [Brandriff et al., 1986; Templado et al., 1988; Martin, 1989, 1992; Pellestor et al., 1989].

The unusual segregation pattern in this family may simply be due to chance. Non-viability of other possible unbalanced segregants may also account for observing only the der(10)t(10;16)((q26.3;p13.1) in all affected offspring. However there is a report [Buckle et al., 1988] of a moderately retarded child with alpha-thalassemia and dysmorphic features who is monosomic for 16p13.3→pter and trisomic for 10q26.13→qter as the result of the unbalanced segregation of a maternal balanced translocation. Although the breakpoint on 10q is slightly more centromeric than in our family, this report implies that the other adjacent I complement, i.e., der(16)t(10;16)(q26.13;p13.3), is viable.

Alternatively, the absence of normal karyotypes may be the result of translocated chromosomes in most or all of the gametes, or enhanced "fertility" of gametes with unbalanced or balanced translocations. Genes for meiotic drive have been reported in mice, mosquitos, *Drosophila,* and *Neurospora* [Lyttle, 1993]. The Sd locus, which produces segregation distortion in *Drosophila,* can be tightly linked to a chromosomal inversion [Lyttle, 1993].

We encourage geneticists to report other families with the same translocation or families with a similar segregation distortion involving different chromosomes.

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